

Symptomatic urinary infection in childhood: presentation during a four-year study in general practice and significance and outcome at seven years

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SUMMARY. Thirty-eight children (12 boys and 26 girls) with symptomatic urinary infection have been studied in general practice. Patients were collected over a four-year period and we report an incidence of urinary infection according to Kass's criterion of 7.7 per 1,000 girls at risk per year and 3.8 per 1,000 boys at risk per year. Eighty-four per cent of the children had symptoms which suggested an origin in the genitourinary tract. *Proteus* infection was found in five of the boys and only one of the girls. At the end of the four-year study period follow-up had taken place over a mean period of 25 months and recurrent infection had been demonstrated in four boys and 12 girls. All the children had an excretion urogram and two children, both girls, were found to have pyelonephritic scarring. Twelve children with recurrent infection were investigated for vesicoureteric reflux, which was found only in the two children with scarring. At seven years 31 of the children remained in the practice and, with a mean follow-up of 42 months, no significant alteration in the figures for recurrent infection was demonstrated. Guidelines are suggested for the management of childhood urinary infection in general practice.

Introduction

A RELATIONSHIP between recurrent urinary infection and radiological evidence of pyelonephritic scarring has been observed only in children

(Hodson and Wilson, 1965). Hospital studies on the presentation and significance of symptomatic childhood infection have been reported (Smellie *et al.*, 1964; Smallpiece, 1966; Bergstrom, 1972) but they have inevitably been carried out on selected populations. Screening studies of bacteriuria in schoolgirls (Kunin, 1970; Savage *et al.*, 1973), and schoolgirls and schoolboys (Cohen and Eirew, 1973) have also been reported, but unselected studies of symptomatic infection by definition need to be carried out in primary medical practice unless it can be said that accurate diagnosis and hospital referral are for all practical purposes invariable. Although many studies of urinary infection in adults have appeared from domiciliary practice (Fry *et al.*, 1962; Loudon and Greenhalgh, 1962; Brooks and Mandar, 1972), with the exception of one study into asymptomatic bacteriuria (Mond *et al.*, 1970) and one public health laboratory study of general-practitioner referrals (Hallett *et al.*, 1976) childhood infection has been neglected.

Method

The practice

The practice is situated in an urban area at the northern edge of the Manchester city boundary. The practice population is unbiased in that it accurately reflects the Registrar General's figures for age and social class for the population of south-east Lancashire as a whole. On 1 July 1969 the practice consisted of 3,908 females and 3,482 males; 838 girls and 794 boys were aged 14 or under, and the total number of patients was the medical responsibility of three principals and one trainee general practitioner.

Criteria

From 1 August 1970 until 31 July 1974 all children under 15 years of age presenting with symptoms that could conceivably be caused by urinary infection, and many other children with vague symptoms in whom a definite diagnosis could not be made, had an 'Oxoid' dip-slide culture of a clean-catch specimen of urine. This was incubated at 37°C on the practice premises for 24 hours. The presence of an organism count > 10⁵ per ml was considered to indicate a urinary infection, this being the sole criterion of infection. A few children provided a second specimen of urine, which in no case altered the diagnosis. The positive dip slides were then taken to a local hospital pathology laboratory where the organisms were subcultured and identified by conventional biochemical tests.

Management

All children with proven urinary infection were seen by one of us (D.B.) and a careful history and general physical examination followed. The medical records were studied and relevant information was collected, in particular details of past illnesses which, with the benefit of hindsight, might have been caused by urinary infection.

All patients received appropriate therapy (usually cotrimoxazole) for ten days, after which a follow-up urine specimen was obtained. Regular follow-up appointments for a period of up to four years were then made. At first these were arranged monthly, but in

those patients in whom a low recurrence rate had been demonstrated, a longer interval was allowed. On these occasions details of intercurrent illnesses were obtained and a urine specimen (handled as before) was taken.

In addition, all patients were referred to a paediatric hospital renal outpatient department, where they were seen by one of us (I.B.H.) for clinical and bacteriological assessment. All patients had excretion urograms, and micturating cystograms were carried out if recurrent infection was demonstrated.

A few patients (four in all) had their urinary infections diagnosed primarily in hospital, having been referred and followed up for reasons usually unconnected with the genitourinary tract.

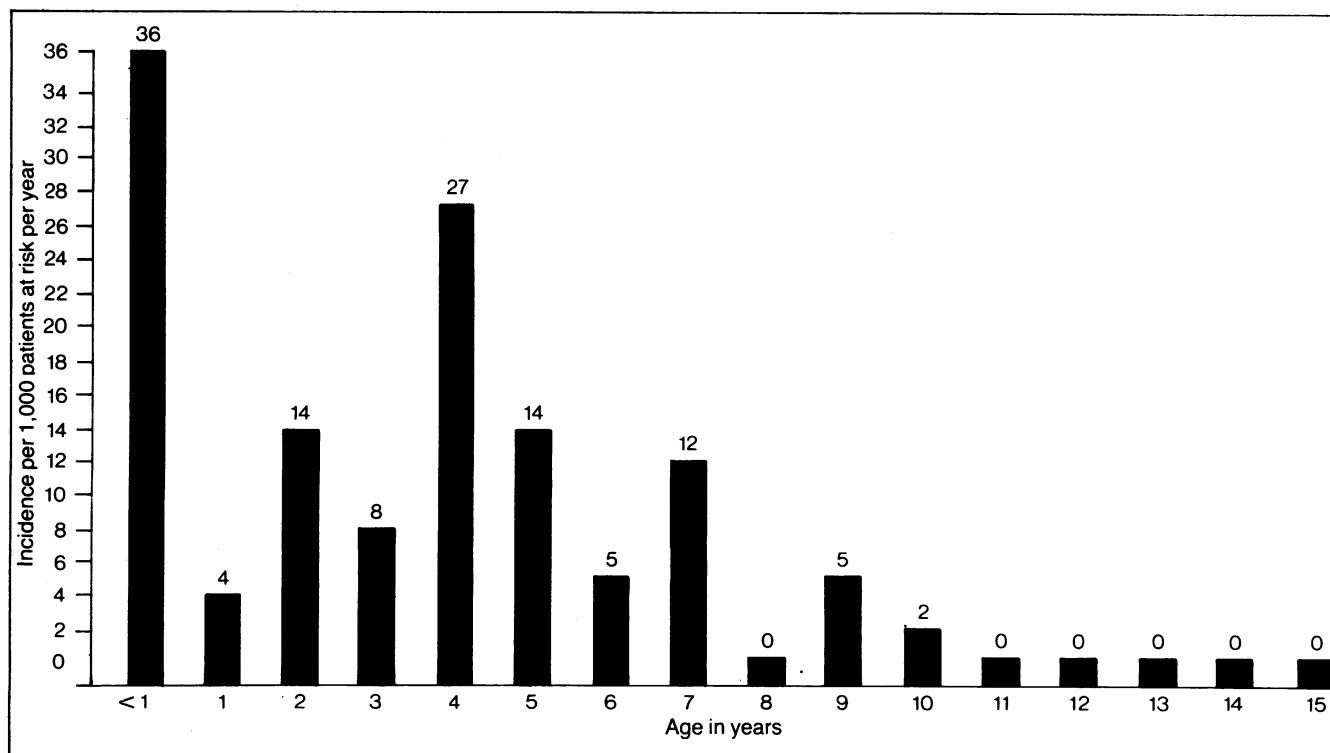
Three years after the end of the study period the records of the children who remained in the practice were studied and relevant details were extracted.

Results

Incidence of infection

Over the four-year study period 38 children in the practice were found to have bacteriologically confirmed urinary infection. We are aware of the diagnosis being suspected on clinical grounds in a further four children, but bacteriological confirmation was not obtained when their urines were examined. Four of the 38 children with infection were diagnosed in hospital rather than in the practice. Of the total of 38 children with infection, 12 were boys and 26 were girls, giving a total incidence of

Figure 1. Age-specific incidence rates (per 1,000 children at risk per year) for 38 children with symptomatic urinary tract infection in general practice.



infection in childhood of 5.8 per 1,000 children at risk per year with a girl:boy ratio of 7.7 per 1,000 to 3.8 per 1,000; that is, 2:1.

Age on entry to the study

The age on entry to the study is presented in Figure 1 as an age-specific incidence rate (i.e. per 1,000 children at risk per year). No children presented between the ages of 11 and 15 and most children were aged seven years or under. With the exception of one boy, aged two, whose acute dysuria and frequency resulted in his mother ringing for an ambulance (the practice doctors were all on their morning visits), all four hospital-diagnosed infections occurred in infants under the age of one year.

Organisms isolated

Thirty-one (82 per cent) of the 38 children had a pure growth of *Escherichia coli* in their urines. Six children (five were boys) had *Proteus* infections. One girl had a mixed infection with *Escherichia coli* and *Streptococcus faecalis*. Thus, 42 per cent of infections in boys were caused by *Proteus* species compared with only four per cent in girls. The girl in question (C.M.) was subsequently found to have an abnormal genitourinary tract.

Presenting features in the children with proven infection

Dysuria, usually associated with frequency of micturition, was present in 27 (71 per cent) of the children, loin pain in three, loin tenderness in two, and vague abdominal pain in 12. Fever was found at the time of the examination or suggested by the history in only eight children. Seven children, according to their mothers, had offensive urine. Nine children had enuresis (defined as bed wetting in children who were normally dry at night) and two children had daytime incontinence; in all cases this was unusual. Haematuria was an unusual symptom, being present in only one girl. One girl had a rigor. None of the children had a raised blood pressure or palpable kidneys.

All these symptoms were, as a rule, of short duration. Only one child had a history of acute symptoms for longer than three days. Only three of the children looked ill and seemed to be seriously upset by their symptoms, but the parents of nine of the children requested a domiciliary visit. All the ill children were seen at home. The history (as obtained spontaneously and by direct questioning) indicated that the urinary tract might be the source of the symptoms in 32 (84 per cent) of the children. Three of the six children with atypical symptoms were infants under the age of one year. One infection was diagnosed in a premature infant who was irritable and failing to thrive in a special care baby unit, and one other, with a feeding problem, was diagnosed at a hospital infant welfare clinic; the third was taken to hospital by her parents after having had a mild convulsion—she had a fever and there was a history of loose stools. The remaining three children

were aged between four and six years; all three complained of vague abdominal pain and one had an associated fever. Ten of the 38 children had suffered previous episodes of symptoms which could have been due to urinary infection, although this is not certain as these symptoms were only characteristic in two and bacteriological examination of a urine specimen had not been carried out. The rest were apparent first attacks.

Associated observations

Five of the 38 children had an associated upper respiratory infection either at the time they presented with the acute urinary infection or within the preceding seven days. Three of the children had chronic constipation and encopresis. Two boys had chronic recurrent balanitis and two girls had recurrent vulvitis. The 38 children with infection included one pair of siblings, and one child had an allergic diathesis.

Recurrent infection

At the end of the study period all children had been followed up for a period of up to four years. The shortest follow-up period was two months and the longest 48 months, with a mean of 25 months and a median period of 18 months. Fifteen children, three boys and 12 girls, had experienced recurrent infection. Nine children had a single recurrence, four children had two recurrences, and two children had four recurrences. Ten of the 25 recurrent infections were symptomatic. The majority were diagnosed in general practice but three children with asymptomatic infection were diagnosed on hospital follow-up. One boy, though asymptomatic, gave frequent low count specimens containing species of *Proteus*.

Further investigation

All 38 children with urinary infection had an excretion urogram; three of these, all females, were reported as abnormal: patients C.M., aged four, S.L.B., aged two, and K.S., aged seven. Patient C.M. had a poorly functioning shrunken left kidney with what appeared to be clubbed calyces probably due to pyelonephritic scarring, although a congenital anomaly could not be excluded. The right kidney was more reasonable in size and functioned better, though one or two calyces looked clubbed and the right ureter was dilated. Patient S.L.B. was found to have a bifid left ureter of which the upper radical was relatively poorly defined and the joint of junction was not apparent. There was a full calyceal pattern on the right. The bladder appeared normal. Further investigation of the renal system appeared to be warranted. Patient K.S. did not demonstrate hydro-nephrosis or hydroureter but there was a straightened right lower pole calyx and inadequate filling of the upper and middle pole calyces on the right side. While the radiologist thought it was probably normal, he considered that a right retrograde pyelogram would be advisable.

Patient C.M. was admitted for cystogram and

cystoscopy. She was found to have gross bilateral vesicoureteric reflux and patulous ureteric orifices. Bilateral ureteric reimplants were performed.

Patient S.L.B. was also admitted for further investigation. Cystoscopy revealed a left-sided ureterocele with an incompetent ureteric orifice above it. Right retrograde catheterisation showed a normal single system with a bifid pelvis. Left-sided catheterisation was not possible. The ureterocele was excised and its ureter brought onto the surface as a separate opening. A second ureter on the left side was incompetent and was freed, mobilized, and then reimplanted. At a second operation three weeks later, in view of the fact that the urine from the upper pole ureter opening onto the surface was not draining, a left heminephroureterectomy was performed. Histology revealed a tortuous ureter reaching 2 cm in diameter in its middle third. The kidney showed pyelonephritis with scarring.

Patient K.S. was admitted for cystoscopy, which revealed some infection over the trigone area. The ureteric orifices were normal and competent. Retrograde pyelography on the right side revealed slightly irregular calyces but the findings were not considered pathological.

Twelve children (32 per cent) had a cystogram but only two of them (C.M. and S.L.B.) were abnormal.

Subsequent progress 1974 to 1977

Although the study period ended in 1974, the records of 31 children involved in the study who remained patients of the practice were examined three years later and details of subsequent urine examinations and other relevant information were extracted. Taking the last recorded urine examination as the end of follow-up the total follow-up period was thereby extended up to a maximum of 58 months and a minimum period of eight months (mean 42 months; median period 33 months). The information resulting from this exercise did not significantly alter the results already reported. With one exception, all the children who originally had recurrent infection remained on the list including the two children with renal scarring, one of whom went on to have three asymptomatic infections during this period. Two of these children with recurrent infection who had already had normal cystograms went on to further episodes of infection. In one girl infection was always symptomatic and occurred on three occasions between 1974 and 1977, the last episode being two years ago, three years after the original infection. One girl originally placed in the non-recurrent group developed an asymptomatic recurrence within two years of the original infection and she was referred for a cystogram which proved to be normal.

Patient S.L.B. This girl was readmitted 12 months after surgery and a cystogram showed a normal bladder, bladder neck, and urethra, and no reflux. Clinically her progress was very satisfactory with no symptomatic

infections and only three asymptomatic infections.

Patient C.M. This girl was also readmitted 12 months after surgery; a cystogram showed a normal bladder with no reflux. Excretion urogram showed quite marked improvement on the right side but there was still a very small scarred kidney on the left, which will probably need to be removed. The dilated right ureter in the original film had disappeared.

Discussion

Little information is available about the incidence of symptomatic childhood urinary infection in general practice. Loudon and Greenhalgh (1962) in a study primarily involving adults identified 16 children over a two-year period, diagnosis being confirmed by a "positive culture at a local laboratory". Incidence rates were reported as 11.3 per 1,000 girls at risk per year and 2.6 per 1,000 boys at risk per year, giving a girl:boy ratio of 4:1 under the age of 15. Fry and his colleagues (1962), studying 13 children and 159 adults identified in 1955, 1956, and 1957, gave a rate of 21.0 per 1,000 girls at risk per year and 7.0 per 1,000 boys at risk per year under the age of ten years, giving a total girl:boy ratio of 3:1. Our rates of 7.7 per 1,000 girls and 3.8 per 1,000 boys at risk per year, giving a sex ratio of 2:1, can be directly compared with the figures reported by Loudon and Greenhalgh, as similar populations (under the age of 15) were reported. We found a slightly lower incidence in girls and a slightly higher incidence in boys, possibly explained in part by different diagnostic criteria. Sex ratios for symptomatic infection in hospital series have been reported as 2.8:1 (Smellie *et al.*, 1964) and 3.3:1 for screening studies (Cohen and Eirew, 1973). We identified only one child with infection between the ages of ten and 15 years, who later developed a follow-up infection at the age of 14. Excluding four infants under one year of age, of whom three were diagnosed in hospital without suprapubic aspiration, most children presented between the ages of two and seven with a peak at four years. The commonest organism isolated was *Escherichia coli*, which was found in 82 per cent of children. Yet out of six children with infection due to *Proteus* species, five were boys; this sex difference failed to reach statistical significance with the numbers involved in this study. However, an increased likelihood of *Proteus* infection in boys has been reported elsewhere (Bergstrom, 1972; Hallett *et al.*, 1976). Bergstrom stated that two thirds of male infections were caused by organisms other than *Escherichia coli*.

Eighty-four per cent of the children had symptoms which suggested an origin in the genitourinary tract, although on occasions these had to be elicited by direct questioning. A similar proportion of typical symptoms was found in a study of urine specimens from boys sent by general practitioners to a public health laboratory (Hallett *et al.*, 1976). The commonest symptoms were

dysuria and frequency, vague abdominal pain, nocturnal enuresis, and offensive urine. Three out of four infants under the age of one year had the vague symptoms described by Smellie and her colleagues (1964). Three older children, however, complained only of vague abdominal pain. Enuresis was an interesting symptom in that although present in nine children, it was rarely the presenting symptom and never a solitary symptom. It was, in fact, often obscured by other symptoms such as fever, dysuria, and frequency and was usually elicited only by direct questioning. Smellie and her colleagues (1964) found that 45 per cent of children in their hospital series had symptoms beginning in the first year of life. Only ten of the children in our group had previous symptoms that might have been due to infection, and these rarely went back quite so far. They found that only 22 per cent of their patients had dysuria and frequency compared with our figures of 71 per cent, and only 30 per cent of their children were referred with the correct diagnosis. Covert symptoms in screening studies were often more characteristic (Savage *et al.*, 1973), but although frequency and urgency and nocturnal enuresis were not uncommon, dysuria was found in only 13 per cent.

Urinary infection in childhood in hospital series often points to underlying renal tract abnormalities. Smellie and her team (1964) found that 13 per cent of children with symptomatic infection had pyelonephritic scarring, and 34 per cent had reflux; these figures were higher when children with recurrent infection were considered separately. However, more recently, Welch and his colleagues (1976) pointed out that infection associated with typical symptoms and minimal reflux can have a good prognosis in terms of renal damage, even when attacks recur frequently.

In our series only two children had pyelonephritic scarring, and of 12 children investigated for reflux only two had this defect. There is evidence, however, that our group differed from the group reported by Smellie and her colleagues in that, as mentioned above, children in the hospital series tended to be younger and have atypical symptoms in a higher proportion of cases; in addition, symptoms could more often be traced back to the first year of life. The relatively low incidence of children aged one, two, and three in our series may reflect the greater difficulty in recognizing illness of any sort in babies, and urinary symptoms in particular; indeed three of four practice children whose infections were diagnosed in hospital were less than 12 months old. It is possible that hospital series tend to contain a higher proportion of clinically atypical infections occurring in a younger population, whereas this general-practice study contained a higher proportion of clinically typical infections, with a lower recurrence rate, limited to the lower urinary tract: children with these infections are probably only rarely referred to hospital. These observations, plus the likelihood that infection and reflux are a greater hazard in the younger child, suggest that our figures for the incidence of

scarring and reflux are not incompatible with hospital series and that large-scale general-practice studies are needed.

When screening studies in the community are considered Savage and his colleagues (1974) found that 35 per cent of primary schoolgirls with urinary infection had reflux and 23 per cent had radiological evidence of pyelonephritis. In general practice Mond and others (1970) investigated eight children with significant bacteriuria, and five had radiological abnormalities. However, screening studies can be expected to be more likely to pick up children with persistent or frequently recurring bacteriuria.

In our series 54 per cent of the girls and 75 per cent of the boys had no recurrence over a mean follow-up period of 25 months, and only one child had a history of acute symptoms lasting longer than three days; only two children had a past history of symptoms actually suggesting urinary infection. In the series published by Savage and his colleagues, however, 70 per cent of the girls had a history of covert symptoms such as frequency, urgency, and nocturnal enuresis.

This study has enabled us to suggest some guidelines for the management of childhood urinary infection in general practice. The significance of the condition has been demonstrated by the discovery of two girls with treatable renal tract lesions: they did not have any particular distinguishing features other than a *Proteus* infection in one case and rapid recurrence of infection in both cases. It seems that all children with urinary tract symptoms and many children with vague symptoms require bacteriological assessment in general practice if those with treatable renal tract lesions are to be identified. The study has demonstrated the feasibility of shared care. Traditional attitudes towards further investigation of children with urinary infection have differentiated between boys and girls in that girls have often been allowed to have more than one infection before undergoing radiological investigation. Since both children with abnormalities in our series were girls we feel that our policy of an excretion urogram in all children after a first attack has been justified. As the children received careful follow-up in general practice as well as at hospital, micturating cystograms and more involved investigations could be delayed, to be carried out in the presence of a pyelographic abnormality or recurrent infection. Since nearly all recurrent infections occurred in the first two years after the original attack, children with infection should be followed up routinely for this period unless reflux has been discovered, when careful follow-up until adolescence is indicated. Much of this follow-up work should take place in general practice and we feel that this study lends further weight to the argument that dip slides and small incubators should be available in all practices.

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Addendum

Since the submission of this paper for publication we have become aware of a large-scale general-practice survey carried out by the Victoria Faculty of the Royal Australian College of General Practitioners involving 135 practitioners (Williams, C. M. (1976) *Australian Family Physician*, 5, 340). Dr Williams reports that urinary infection was found in 24 per cent of children who admitted to symptoms of frequency and dysuria, and of 116 children with proven infection investigated radiologically 36 had an abnormality of some sort, most commonly reflux. Three children were found to have serious bilateral renal disease.

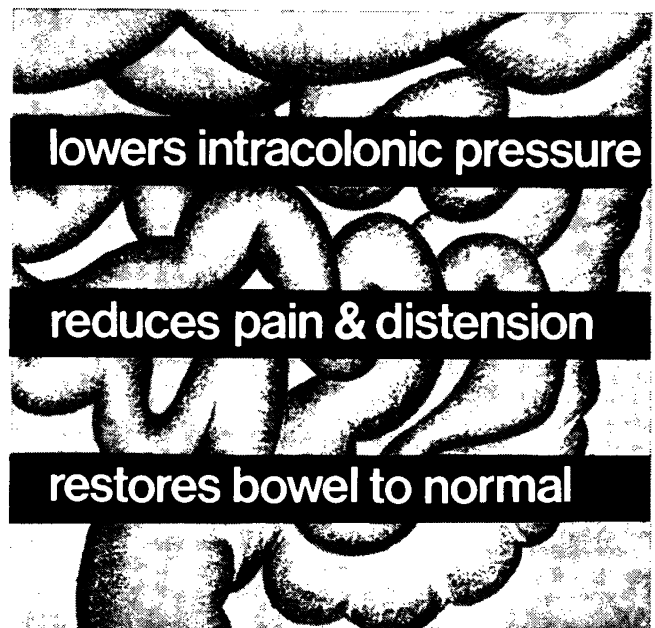
Mortality among oral contraceptive users

In a large prospective study carried out in the UK, the death rate from diseases of the circulatory system in women who had used oral contraceptives was five times that of controls who had never used them. The death rate in those who had taken the Pill continuously for five years or more was ten times that of the controls. The excess deaths in oral contraceptive users were due to a wide range of vascular conditions. The total mortality rate in women who had ever used the Pill was increased by 40 per cent and this was due to an increase in deaths from circulatory diseases of one per 5,000 ever-users per year. The excess was substantially greater than the death rate from complications of pregnancy in the controls, and was double the death rate from accidents. The excess mortality rate increased with age, cigarette smoking, and duration of oral contraceptive use.

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